Impaired scaling of responses to vestibular stimulation in incomplete SCI

Wydenkeller, S ; Liechti, M ; Müller, R ; Curt, A

Abstract: Patients with incomplete spinal cord injury (iSCI) have impaired postural control leading to a high danger of falling. Clinically, it is impossible to assess the extent to which postural instability due to sensorimotor deficit is influenced by a disturbance in the vestibulospinal pathways. Galvanic vestibular stimulation (GVS) was applied to investigate changes in the vestibular spinal responses and their potential influence on postural stability in iSCI patients. Six chronic iSCI patients and age-matched controls were stimulated with a bipolar binaural stimulus. The centre of pressure (CoP) and soleus EMG responses during free standing with closed eyes on firm and compliant ground were measured. The impairment in postural stability was assessed by the mean amplitude of CoP deflections during two minutes undisturbed standing. Although iSCI patients were significantly less stable than controls, direct GVS responses of the soleus EMG and postural sways tended to be increased on firm ground. The GVS responses increased when changing from firm to compliant ground, showing a close correlation between the extent of postural instability and the response amplitudes. Therefore, challenging proprioceptive feedback induced a significant up-modulation of the GVS responses. However, when we took the postural instability in iSCI patients into account, the EMG and CoP responses to GVS were reduced compared to controls. The combined assessment of EMG and CoP responses to GVS complements the clinical examination and permits evaluation of the preservation and modulation of vestibulospinal responses in iSCI

DOI: https://doi.org/10.1007/s00221-006-0688-z

Exp Brain Res (2006) 175:191–195
DOI 10.1007/s00221-006-0688-z

RESEARCH NOTE

Impaired scaling of responses to vestibular stimulation in incomplete SCI

S. Wydenkeller · M. Liechti · R. Müller · A. Curt

Received: 22 March 2006 / Accepted: 24 August 2006 / Published online: 28 September 2006

Abstract Patients with incomplete spinal cord injury (iSCI) have impaired postural control leading to a high danger of falling. Clinically, it is impossible to assess the extent to which postural instability due to sensorimotor deficit is influenced by a disturbance in the vestibulospinal pathways. Galvanic vestibular stimulation (GVS) was applied to investigate changes in the vestibular spinal responses and their potential influence on postural stability in iSCI patients. Six chronic iSCI patients and age-matched controls were stimulated with a bipolar binaural stimulus. The centre of pressure (CoP) and soleus EMG responses during free standing with closed eyes on firm and compliant ground were measured. The impairment in postural stability was assessed by the mean amplitude of CoP deflections during two minutes undisturbed standing. Although iSCI patients were significantly less stable than controls, direct GVS responses of the soleus EMG and postural sways tended to be increased on firm ground. The GVS responses increased when changing from firm to compliant ground, showing a close correlation between the extent of postural instability and the response amplitudes. Therefore, challenging proprioceptive feedback induced a significant up-modulation of the GVS responses. However, when we took the postural instability in iSCI patients into account, the EMG and CoP responses to GVS were reduced compared to controls. The combined assessment of EMG and CoP responses to GVS complements the clinical examination and permits evaluation of the preservation and modulation of vestibulospinal responses in iSCI.

Keywords GVS · Vestibulospinal responses · SCI · Posture

S. Wydenkeller · M. Liechti · R. Müller (✉) · A. Curt
Spinal Cord Injury Center, Balgrist University Hospital,
Forchstrasse 340, 8008 Zurich, Switzerland
e-mail: roland.mueller@paralab.balgrist.ch

A. Curt
Division of Neurology/Department of Medicine and ICORD,
University of British Columbia,
2469-6270 University Boulevard,
Vancouver, BC, V6T 1Z1Canada

Introduction

Balance is an important problem for a majority of ambulatory patients with incomplete spinal cord injury (iSCI). Indeed, they suffer from an increased danger of falls. Clinically, it is difficult to assess the contribution of each of the spinal tracts underlying postural instability. While the function of somatosensory or motor tracts is routinely evaluated with electrophysiological methods (Curt and Dietz 1999), the assessment of vestibulospinal pathways in SCI patients is not yet established.

A possible means to assess the integrity of the vestibulospinal pathways is with galvanic vestibular stimulation (GVS). During GVS a constant direct current is applied to the vestibular system through electrodes placed over one or both mastoids. GVS elicits a distinct pattern of body sway and excitatory or inhibitory EMG responses of short (SL) or medium (ML) latency in posturally active muscles (Britton et al. 1993). The motor centres involved in the vestibulospinal reflex response integrate afferent inputs from

many sources in addition to the vestibular system. Therefore, GVS responses are strongly influenced by changes in somatosensory or visual information (Britton et al. 1993). The significant impact of impaired proprioceptive feedback on GVS responses could be shown in patients suffering from peripheral neuropathy (Horak and Hlavacka 2001). In these patients, the disturbance in proprioceptive input leads to a greater reliance on the vestibular system and accordingly, GVS responses are larger. In addition, GVS responses are greater when proprioceptive input is attenuated by standing on compliant ground (Welgampola and Colebatch 2001).

So far only one study has examined vestibulospinal reflexes in SCI patients (Iles et al. 2004). GVS-elicited EMG responses in the back muscles (erectores spinae) of SCI patients had reduced amplitudes and delayed responses compared to control. GVS-induced responses were also related to the extent of injury as defined by the ASIA Impairment Scale (Maynard et al. 1997).

In the present study, we investigated GVS-elicited lower limb EMG and postural responses in people with iSCI to assess: (1) the preservation of the vestibulospinal pathways in iSCI and (2) how changes in proprioception (either due to somatosensory deficit or challenging ground condition) modulate GVS responses.

Method

Subjects

Six male ambulatory iSCI patients (SCI; age 57 ± 9 years; height 1.81 ± 0.04 m; weight 83 ± 12 kg; mean ± S.D.) and gender- and age-matched healthy controls (C; age 57 ± 10 years; height 1.78 ± 0.03 m; weight 81 ± 8 kg) participated. All patients had chronic, incomplete tetraplegia, classified as ASIA D grade (Maynard et al. 1997) but with varying lesion levels. All iSCI subjects were able to stand freely with eyes closed for at least three minutes. All subjects participated with informed consent and the approval of the local ethics committee according to the Declaration of Helsinki.

Setup

In the firm ground condition (SCI-FG and C-FG), subjects stood on a force platform (Kistler Instrumente, Switzerland). In the compliant ground condition (SCI-CG and C-CG), subjects stood on a 6 cm thick balance cushion (Airex Balance Pad, Alcan Airex AG, Switzerland) placed on the platform.

To prevent falling, subjects were secured with a safety harness attached to the ceiling. The suspension was adjusted loosely in order to minimise sensory input from leaning on the harness straps due to small positional skews. Subjects stood upright facing forwards, the arms folded in front of the chest, the eyes closed and the feet positioned 15 cm apart.

Stimulation

Stimulation electrodes (50 × 50 mm, Synapse, Denmark) were placed over both mastoids. A Compex2 stimulator (Compex Medical SA, Switzerland) with Compex Motion Software (Keller et al. 2002) was used to stimulate the vestibular system with an uniphasic binaural bipolar stimulus of 4 mA amplitude and 400 ms duration. Stimuli were delivered randomly with respect to stimulus polarity and inter-stimulus interval (6–10 s).

Electromyographic activity

Myoelectric activity was measured over both soleus muscles with surface electrodes (Ag/AgCl). A reference electrode was put around the right ankle. Signals were pre-amplified 500× and bandpass-filtered (16–500 Hz) before additional amplification and recording with a PC at a sampling rate of 2,000 Hz. Data acquisition and analysis were performed with Soleasy (ALEA Solutions, Switzerland).

The EMG data were rectified before being filtered again (lowpass 40 Hz). The mean activity over 100 ms before stimulus onset was subtracted from all values. EMG data were then normalised to the average EMG recorded during a maximal voluntary contraction against manual resistance. The amplitudes and onset latencies of the first and the second deviation of the curve from the baseline (SL and ML responses, respectively) were determined from the average of responses from the ipsi- and contralateral (relative to the anode) soleus muscles. That way one combined value for a total of 60 stimulations was attained. The latencies were normalised to height of the subjects.

Body Sway

Force data were recorded with the PC at a sampling frequency of 500 Hz. The mean amplitude of the CoP during two minutes of quiet standing during both the FG and CG conditions was calculated as a measure for standing stability (Hufschmidt et al. 1980). As a measure of sway during GVS, only values of lateral displacement were considered since the anteroposterior

sway was negligible in this setting. Thirty responses to each polarity were averaged (see Fig. 1) and the polarities were pooled to determine the onset latencies and amplitudes of the first three deviations from the baseline (ay1, ay2 and ay3, see Fig. 1). The latencies were normalised to height of the subjects.

Statistical analysis

The measurement parameters were tested for differences between values of controls and patients using a two way ANOVA with Bonferroni correction. For testing the differences between the mean amplitudes of CoP deflection during undisturbed standing, a *t*-test was applied. A Pearson correlation analysis was performed in order to investigate the relationship between the measurement parameters and standing stability. The significance level was set to 5%.

Results

In general, body sway was more reliably recorded than EMG responses. The very early SL EMG responses and the early CoP changes were especially difficult to record in both the controls and patients (see Table 1). All subjects had smaller responses on firm compared to compliant ground. Except for the correlation analysis, only subjects who showed responses on compliant as well as on firm ground were included in the statistical analysis, for attaining a consistent sample group (number of subjects included in the statistical analysis: see Table 1).

The EMG response to GVS was biphasic and consisted of SL and ML components as well as a biphasic

Table 1 Excitability of the EMG and body sway responses to GVS

	EMG				CoP					
	SL		ML		ay1		ay2		ay3	
	CG	FG	CG	FG	CG	FG	CG	FG	CG	FG
C1	–	+	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**
C2	**+**	**+**	**+**	**+**	–	+	**+**	**+**	**+**	**+**
C3	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**
C4	+	–	+	–	–	+	**+**	**+**	**+**	**+**
C5	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**
C6	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**
##	4		5		4		6		6	
SCI1	+	–	+	–	**+**	**+**	**+**	**+**	**+**	**+**
SCI2		+		+		+		+		+
SCI3	**+**	**+**	**+**	**+**	+	–	**+**	**+**	**+**	**+**
SCI4	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**
SCI5	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**
SCI6	+	–	+	–	+	–	**+**	**+**	**+**	**+**
##	3		3		3		5		5	

+ Normal excitability, – no excitability; bold if excitable on firm (FG) and compliant (CG) ground. ## number of values used for analysis; *SL* short-latency, *ML* medium-latency response, *ay1*, *ay2*, *ay3* three components of the CoP deviation

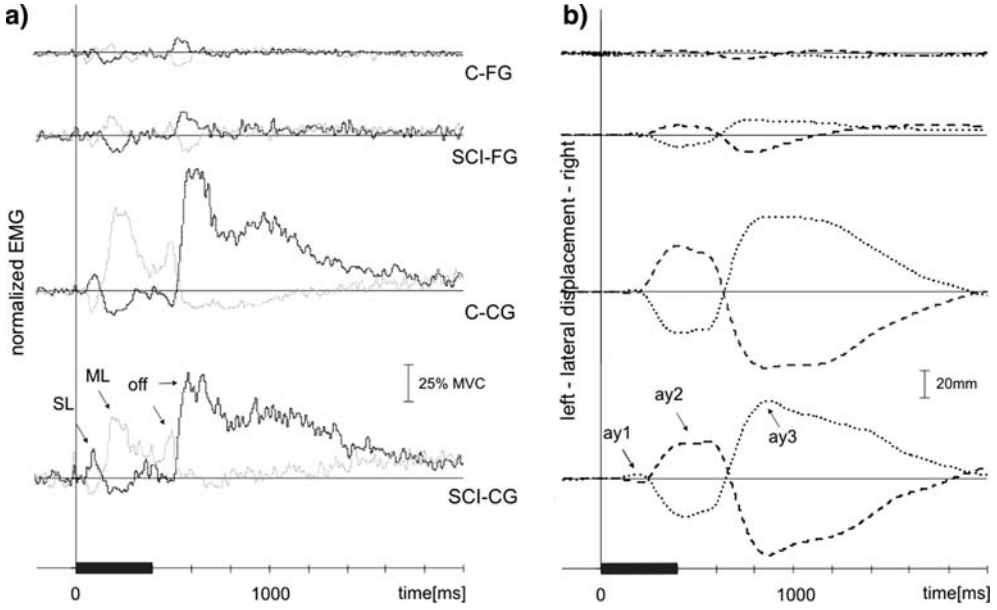

Fig. 1 Mean of all measured subjects. **a** EMG short-latency (SL) and medium-latency (ML) response, off-response (OFF) of the ipsilateral (*black*) and contralateral (*grey*) soleus muscles (relative to the anode). MVC: maximal voluntary contraction against manual resistance. **b** Three components of the CoP response ay1, ay2 and ay3. The anode was either on the right (*dotted*) or on the left (*dashed*) mastoid. iSCI patients on firm ground (SCI-FG), controls on firm ground (C-FG), iSCI patients on compliant ground (C-FG), controls on compliant ground (C-CG). Bar at the bottom: stimulus duration

off-response upon stimulus offset. The SL EMG response was opposite in sign to the accompanying ML response. The CoP response was triphasic (ay1, ay2 and ay3; see Fig. 1). The EMG and the CoP responses were reversed if stimulus polarity was switched.

Standing on FG, EMG and CoP amplitudes tended to be larger in iSCI than in controls and to be smaller when standing on CG. However, no significant differences resulted (see Fig. 2). The EMG latencies were not significantly different from each other, although the latencies measured in patients tended to be longer. The CoP deviation latencies were all longer for patients than for controls but none were significantly different.

A correlation analysis between the mean CoP amplitude during quiet standing and the induced GVS responses (mean EMG and CoP deflections) produced several significant correlations (see Table 2), indicating that GVS response amplitudes and latencies scaled up with increasing instability. The mean amplitudes for CG were significantly larger than for FG, for both the iSCI ($P < 0.05$) and control group ($P < 0.01$), whereas the mean amplitudes were not statistically different between SCI-FG and C-CG ($P = 0.45$).

By comparing the responses of SCI-FG and C-CG the results were corrected for instability since iSCI patients on FG and controls on CG showed a similar standing stability during a two minutes standing test. The comparison revealed significantly larger ay2 ($P = 0.005$) and ay3 ($P = 0.002$) amplitudes in the controls than in the iSCI patients (see Fig. 2). The EMG amplitudes were not significantly different, although the ML amplitude tended to be larger in the control group. The latencies showed no consistent differences between the two groups.

Table 2 Correlation coefficients

	Pearson coeff	*P*
Amplitude		
SL	0.40	0.065
ML	0.40	0.062
ay1	0.70	0.000
ay2	0.60	0.001
ay3	0.64	0.000
Latency		
SL	0.54	0.008
ML	0.55	0.007
ay1	0.47	0.014
ay2	0.77	0.000
ay3	0.65	0.000

Correlation coefficients between the mean centre of pressure (CoP) amplitude during two minutes undisturbed standing and the response parameters after galvanic vestibular stimulation with *P*-value

Discussion

In standing iSCI patients, early EMG and CoP responses can be excited comparable to controls. The GVS responses were strongly correlated to postural stability and increased when standing on challenging ground. However, if the increase of GVS responses were corrected for postural instability, the EMG and CoP responses were reduced in iSCI patients compared to controls.

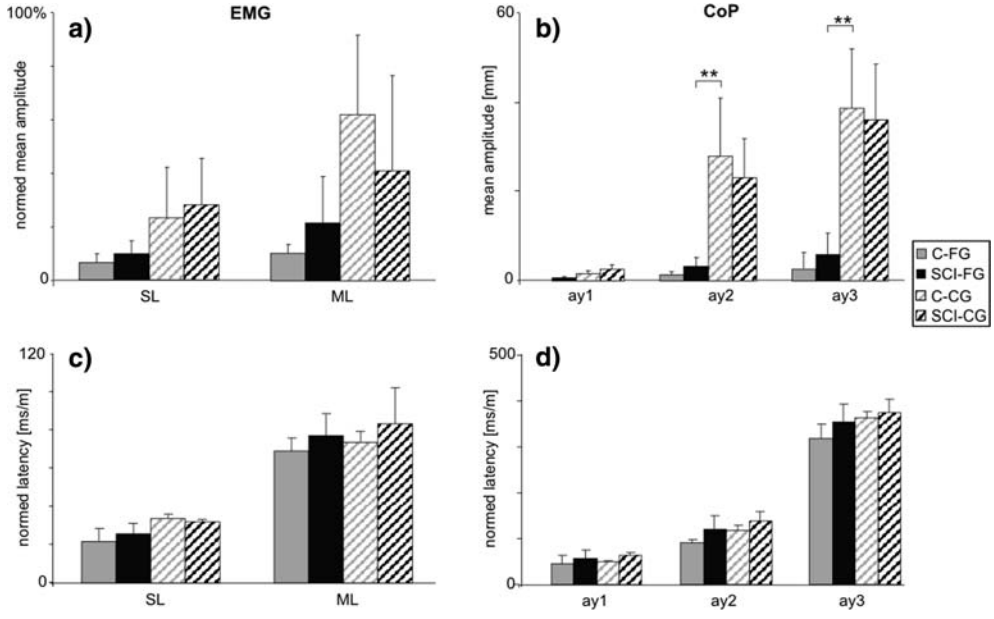

Fig. 2 **a** Mean normalised EMG amplitude; *left* short-latency; *right* medium-latency; **b** Mean CoP deviation amplitude; *left* ay1, *middle* ay2, *right* ay3; **c** EMG latencies; *left* short-latency, *right* medium-latency; **d** CoP deviation latency; *left* ay1, *middle* ay2, *right* ay3. $*P < 0.05$; $**P < 0.01$; *n* see ## in Table 1. Significancies are shown for comparisons between groups only

While the early EMG responses permit assessment of the direct vestibulospinal pathways, the influence of the combined afferent and efferent impairment in iSCI on the compensatory reaction to vestibulospinal perturbations cannot be distinguished. The present study showed preserved early GVS responses in iSCI patients. The analysis of the median and late EMG and CoP responses disclosed delayed and reduced responses.

The measured soleus EMG records in controls are in agreement with previous data (Ali et al. 2003). The only published data of GVS in SCI patients showed that patients with more severe impairment had longer latencies and smaller amplitudes of back muscle EMG responses (Iles et al. 2004). Even though they cannot simply be related because of different paradigms with standing or sitting subjects, respectively, those findings are in line with the present results. According to the results of Iles et al. the delay of the median and late responses could be considered to be due to either a changed central processing or a slowed spinal conduction.

Comparably to patients suffering from diabetic polyneuropathy and therefore impaired sensory feedback, iSCI patients showed larger CoP deviations upon GVS on FG than controls (Horak and Hlavacka 2001). The important influence of sensory input on GVS responses is also evident in iSCI patients when challenging the sensory feedback by changing from firm to foam ground (Welgampola and Colebatch 2001). However, when correcting the increase of GVS responses by the amount of postural instability, iSCI patients have a less upscaling of the responses compared to healthy controls. This finding could indicate that in iSCI patients compensatory postural reactions are restricted as they depend on combined sensory and motor reactions. This corroborates to the clinical finding of increased postural instability in iSCI with a higher danger of falls.

In SCI repair/regeneration research, the study of the vestibulospinal efferents are of potential interest since these motor pathways could become involved in functional recovery - either through increasing their influence on motor functions or becoming a conduit for descending motor commands and bypassing a spinal lesion (Bareyre et al. 2004).

The present study measured vestibulospinal responses in posturally active muscles. Such a setup excludes the possibility of investigating iSCI patients who are not able to stand. Additionally, the clinical status of the patients was quite good, perhaps foreclosing the finding of larger differences between patients and controls. Although the measured latencies and amplitudes showed differences between the groups, only few were significant, this could be attributable to the small sample sizes. Coming research should try to broaden the applicability of these investigations to more severely affected patients including acute SCI, possibly by the integration of reflex studies (Kennedy et al. 2004).

Acknowledgments This study was supported by the National Centre of Competence in Research (NCCR) on Neural Plasticity and Repair and the International Spinal Research Trust (ISRT, Grant no. CLI006). We would like to thank T. Lam for her contribution to this work.

References

Ali AS, Rowen KA, Iles JF (2003) Vestibular actions on back and lower limb muscles during postural tasks in man. J Physiol 546:615–624

Bareyre FM, Kerschensteiner M, Raineteau O, Mettenleiter TC, Weinmann O, Schwab ME (2004) The injured spinal cord spontaneously forms a new intraspinal circuit in adult rats. Nat Neurosci 7:269–277

Britton TC, Day BL, Brown P, Rothwell JC, Thompson PD, Marsden CD (1993) Postural electromyographic responses in the arm and leg following galvanic vestibular stimulation in man. Exp Brain Res 94:143–151

Curt A, Dietz V (1999) Electrophysiological recordings in patients with spinal cord injury: significance for predicting outcome. Spinal Cord 37:157–165

Fitzpatrick R, McCloskey D (1994) Proprioceptive, visual and vestibular thresholds for the perception of sway during standing in humans. J Physiol 478:173–186

Horak FB, Hlavacka F (2001) Somatosensory loss increases vestibulospinal sensitivity. J Neurophysiol 86:575–585

Hufschmidt A, Dichgans J, Mauritz KH, Hufschmidt M (1980) Some methods and parameters of body sway quantification and their neurological applications. Arch Psychiatr Nervenkr 228:135–150

Iles JF, Ali AS, Savic G (2004) Vestibular-evoked muscle responses in patients with spinal cord injury. Brain 127:1584–1592

Keller T, Popovic MR, Pappas IPI, Muller PY (2002) Transcutaneous functional electrical stimulator "Compex Motion". Artif Organs 26:219–223

Kennedy PM, Cresswell AG, Chua R, Inglis JT (2004) Vestibulospinal influences on lower limb motoneurons. Can J Physiol Pharmacol 82:675–681

Maynard FM Jr, Bracken MB, Creasey G, Ditunno JF Jr, Donovan WH, Ducker TB, Garber SL, Marino RJ, Stover SL, Tator CH, Waters RL, Wilberger JE, Young W (1997) International standards for neurological and functional classification of spinal cord injury. American spinal injury association. Spinal Cord 35:266–274

Welgampola M, Colebatch J (2001) Vestibulospinal reflexes: quantitative effects of sensory feedback and postural task. Exp Brain Res 139:345–353